

What is claimed is:

43. A once-a-day controlled absorption diltiazem pellet formulation for oral administration comprising a blend of long lag and short lag pellets, each of said pellets comprising:

(a) a core comprising 18% to 34% sugar spheres, 60% to 80% diltiazem hydrochloride and 2 to 6% hydroxypropylcellulose, expressed as percentages of the total weight of the core, said core being substantially free of organic acid, the amount of any such organic acid being sufficiently small so as not to substantially affect the release rate of diltiazem hydrochloride from the core, and

(b) a single coating layer having a thickness surrounding said core, each coating layer consisting essentially of 31% to 35% talc, not more than 8% sodium lauryl sulfate, not more than 8% triethyl citrate, 2% to 7% of a first copolymer of acrylic and methacrylic acid esters, and 53% to 59% of a second copolymer of acrylic and methacrylic acid esters, expressed as percentages of the total weight of the coating layer, the first copolymer being permeable to water and diltiazem, the second copolymer being less permeable to water and diltiazem than said first copolymer, the thickness of the coating layer surrounding the long lag pellet core being greater than the thickness of the coating layer surrounding the short lag pellet core such that the diltiazem from the core of the short lag pellets is released before the diltiazem from the core of the long lag pellets, the thicknesses of said coating layers of said short and long lag pellets being effective to permit the release of a therapeutically effective amount of said diltiazem from said pellet formulation at a rate allowing controlled absorption thereof over, on

the average, a twenty-four hour period following oral administration, said rate being measured in vitro as a dissolution rate of said pellets, which when measured in a type 2 dissolution apparatus (paddle) according to the U.S. Pharmacopoeia XIII in 0.1N HCl at 100 rpm substantially corresponds to the following dissolution pattern:

- a) not more than 10% of the total diltiazem is released after 1 hour of measurement in said apparatus;
- b) from 20% to 45% of the total diltiazem is released after 6 hours of measurement in said apparatus;
- c) from 35% to 45% of the total diltiazem is released after 8 hours of measurement in said apparatus;
- d) from 35% to 45% of the total diltiazem is released after 11 hours of measurement in said apparatus;
- e) not less than 85% of the total diltiazem is released after 18 hours of measurement in said apparatus; and
- f) not less than 90% of the total diltiazem is released after 24 hours of measurement in said apparatus.

44. The diltiazem pellet formulation of claim 43, wherein said short lag pellets, when measured in a type 2 dissolution apparatus (paddle) according to the U.S. Pharmacopoeia XXIII in 0.1N HCl at 100 rpm, exhibit the following in vitro dissolution profile: not more than 10% of the total diltiazem is released after 1 hour, 50% of the total diltiazem is released

between 3 and 4 1/2 hours, and not less than 85% of the total diltiazem is released after 8 hours; and said long lag pellets, when measured in a type 2 dissolution apparatus (paddle) according to the U.S. Pharmacopoeia XXIII in 0.1N HCl at 100 rpm, exhibit the following in vitro dissolution profile: not more than 5% of the total diltiazem is released after 1 hour, 50% of the total diltiazem is released between 12 and 16 hours, and not less than 85% of the total diltiazem is released after 18 hours.

45. The pellet formulation of claim 43, wherein the core further comprises at least one of a dispersing agent, a glidant and a surfactant.

46. The pellet formulation of claim 44, wherein the core further comprises at least one of a dispersing agent, a glidant and a surfactant.

47. A capsule or tablet formulation comprising pellets according to claim 43.

48. A capsule or tablet formulation comprising pellets according to claim 44.

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